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A randomized control trial to gauge the efficacy of leucocyte rich platelet rich plasma (LR-PRP) injection versus local corticosteroid injection in treatment of plantar fasciitis

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Abstract
Introduction: Heel pain due to plantar fasciitis is a common problem which leads to a significant morbidity and belittled quality of life. Various treatment ways have been tried in dealing with this problem with varying efficacy rates. The current study was planned to evaluate the efficacy of Leucocyte rich platelet rich plasma (LR-PRP) injections when compared to traditional therapy with corticosteroid injections in patients with plantar fasciitis.
Methods: Patients with a history of plantar fasciitis were block randomized into 2 groups (n=30 in each). The first group was subjected to Leucocyte rich platelet rich plasma injections whereas the other underwent corticosteroid injections. The patients were followed up for 6 months at intervals of 1, 4, 12 weeks and at the end of 6 months the treatment outcome was evaluated using visual analogue score and Nirschl staging system.
Results: At the end of 6 months 46.66% patients in corticosteroid injection group and 90% patients in LR-PRP group were completely relieved of pain. The duration for maximum benefit to reach is longer in LR-PRP (11.43weeks) compared to corticosteroid injection (6.1 weeks).
Discussion: Patients on Leucocyte rich platelet rich plasma demonstrated a statistically significant decrease in pain compared to corticosteroid injection group on 6 month follow up. It can be concluded that LR-PRP does seem to provide an alternative treatment strategy providing better pain relief in patients with plantar fasciitis on a long-term basis with minimal side effects.

Keywords: leucocyte rich platelet rich plasma; plantar fasciitis; corticosteroid injections; randomized control trial; pain

Introduction
Plantar fasciitis is a very common orthopedic problem involving inferior heel pain [1]. It's said to cause pain in both active and inactive adults across ages [2]. To describe pain under the plantar aspect of the heel various terminologies have been used till date. This includes terms like gonorrhoeal heel, Policeman's heel, heel spur syndrome, subcalcaneal pain, jogger's heel, plantar fasciitis, plantar fasciopathy, plantar fasciosis and plantar heel pain [3]. Plantar fasciitis is defined as localized inflammation and degeneration of the proximal plantar aponeurosis, with the most commonest site being near the origin at the medial tuberosity of the calcaneus (Figure 1) [4]. The classic presentation of the problem involves patients complaining of heel pain when getting out of their beds in the morning or after prolonged sitting [5, 6].
Risk factors for plantar fasciitis include obesity [5, 7], work related weight bearing [5], reduced dorsi-flexion of ankle [8]. Clinical management of plantar fasciitis includes nonsurgical methods like rest, massage, non-steroidal anti-inflammatory drugs, night splints [9], heel cups/ pads, custom and off the shelf orthoses, steroid injections [10], casts, and physical therapy measures such as shock wave therapy [11]. Effectiveness of these therapies have not been consistent [12]. A Cochrane database review found not much significant reduction in heel pain in patients subjected to local steroid injections as compared to those on placebos or on no treatment. They found the method be effective in reducing heel pain for one month and not later than that [10].
Recently Platelet rich plasma (PRP) injected locally has evolved as a new strategy in treatment of plantar fasciitis [13, 14]. PRP has been used in treatment of various sports injuries also. There are studies which have reported benefits of PRP injections and there are studies that have reported no benefit if this. In a multicentric trial of PRP injections on sports persons with hamstring injury did not find significant benefit of this therapy [15]. In a study on plantar fasciitis PRP injections were found to be better at achieving symptomatic relief on par with steroid injections at 3 and 6 months after injections. Moreover PRP was found to be more effective after 12 months of injections compared to steroids [13]. PRP preparations have been recently classified into four types based on fibrin architecture and cell content. They are namely Pure Platelet-Rich Plasma, Leukocyte- and Platelet-Rich Plasma, Pure Platelet-Rich Fibrin and Leukocyte and Platelet-Rich Fibrin [16]. The presence of white blood cells in platelet rich plasma has elicited conflicting views with regard to its efficacy. Some studies have shown the beneficial effect of white blood cells in

PRP. Growth factor concentrations have been reported to be dependent on the leukocyte concentrations in the PRP [17]. The presence of leukocyte has been reported to increase the antimicrobial and immunological resistance due to the release of pro-inflammatory cytokines [18]. Even though many studies have reported the use of PRP in plantar fasciitis, not many studies from India have reported the use of L-PRP for same. It was hypothesized that mitogens such as Platelet Derived Growth Factor (PDGF) induce fibroblastic mitosis and chemotactic polypeptide such as transforming growth factor cause fibroblast to migrate and helps in healing.

The present study is designed with the intention to evaluate the efficacy and role of L -PRP in plantar fasciitis and to compare this with the effect of local injection of corticosteroid (CI) which is very often used in clinical practice.

Subject and Methodology

The study was conducted in the department of Orthopedics, Yenepoya Medical College, Yenepoya University, Mangalore, India. Permission for the present study was obtained from the Institute Ethics committee (IEC). All study participants gave written informed consent.

In this prospective randomized study we included 60 patients who had reported to the Orthopedics department complaining of heel pain. The patients were allocated to the two study groups after complete physical examination including heel pain and tenderness over the plantar medial aspect of the calcaneal tuberosity, near the insertion of the plantar fascia and assessing the history. Block randomization was used to allocate patients to the two group namely the steroid injection group (n = 30) LR-PRP group (n = 30).

In the present study leukocyte rich PRP was used. This is a preparation of PRP with leucocytes and with low-density fibrin network after activation [19].

Method of injection

Leucocyte rich platelet-rich plasma injection procedure

Under aseptic condition, venipuncture was performed and IV canula was secured to the skin. 30 ml blood was drawn into syringe containing 2 ml of anticoagulant Citrate Dextrose Solution (Figure 2) – Formula A (ACD-A) and adequately mixed to make the total volume 60 ml.

Fig 2

Methodology for preparing LR-PRP: Differential centrifugation method was used in preparation of LR-PRP. This method used the specific gravity of various components in blood for their separation and sedimentation. Centrifugation was done in two stages. In the first step the red blood cells were removed and in the second platelet concentrate was prepared.

Fig 2

Whole blood collected under aseptic condition in process disposable (TriCell Biologics, India,) containing anticoagulant attached sswith wide bore needle was first centrifuged to separate the RBCs. For producing LR-PRP, the entire layer of buffy coat containing platelets, white blood cells and few RBCs were pushed in the upward direction in order to lock the chamber of RBCs. Later the plasma and LR-Rich platelets were suspended and centrifuged as per the manufacturer's direction (Figure – 4 & 5).

In the present study FLETA -P40 (Figure 3) centrifuge specially made for PRP preparation was used. The machine provides sufficient 'g' so that during the second spin erythrocyte -platelet pellets are formed easily.

Fig 4

Fig 5

A technique called peppering [20, 21] was used in administering the LR-PRP to the patients in the LR-PRP group (Figure 6). Following the administration of LR-PRP patients were advised to avoid strenuous activities & rest for 2 weeks.

Fig 6

Corticosteroid injection procedure

Under aseptic precautions, patients in the steroid injection group received 2 ml local corticosteroid (methylprednisolone acetate 80mg) + 1ml 0.5% Bupivacaine at the anterio-medial aspect of calcaneum which is the origin of plantar fascia, followed by occlusive dressing and patient was mobilized (Figure 7).

Fig 7

Follow-Up of the patients were done for 6 months at intervals of 1 week, 4-week, 12 week and 6 months. Outcome in terms of pain relief was assessed using Visual analogue score [22] and Nirschl staging system [23].

Statistics

IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp. was used for statistical analysis. Mann Whitney U test (nonparametric) was used to assess significance of the results.

Results

At the beginning of the study patients in both LR-PRP group and steroid injection group had VAS of 7.5 & 7.6 respectively. At 1 week and 4 weeks the steroid injection group showed a statistically significant decrease in pain compared to LR-PRP group. Whereas after 12 weeks and 6-months follow-up LR-PRP group showed statistically significant decrease in pain compared to steroid group. The reduction in pain in steroid group was rapid but lasted only 4 weeks and then tapered off. Whereas the pain reduction in LR-PRP group was slow but long lasting throughout the course of the follow up. This probably highlighted the long-term effectiveness of LR-PRP in pain relief.

Nirschl staging system scores at the beginning if the study in two groups were 5.3 (for both). At 4th week it dropped to 1.3 in steroid group and then leveled off at 12 weeks and 6 months follow-up, whereas in LR-PRP group it took 12 weeks for a significant fall and remained the same at 6 months also.

Maximum pain relief was obtained faster in steroid group (6.1 weeks) as compared to 11.43 weeks in LR-PRP group. Contrarily the recurrence of pain was more in steroid group as compared to LR-PRP group. At the end of 6 months 46.66% [n= 14] patients in steroid injection group and 90% patients [n = 27] in LR-PRP group were completely relieved of pain.

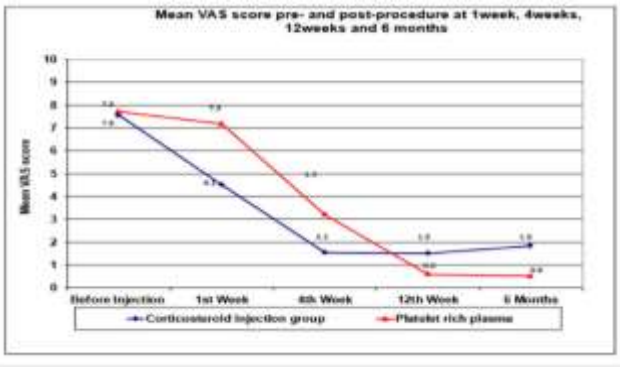

Fig 8: Mean VAS Score between Corticosteroid group and Platelet rich plasma gro

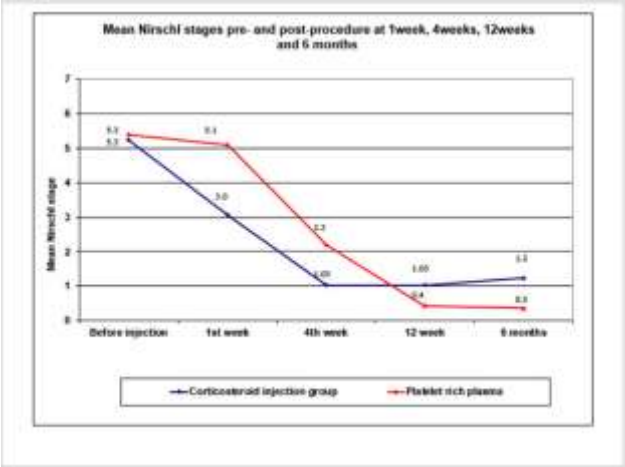

Fig 9: Mean Nirschl stages of Corticosteroid group and Platelet rich plasma group.

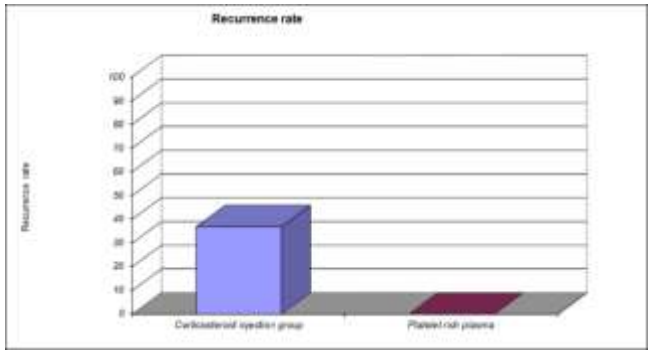

Fig 10: Rate of recurrence between Corticosteroid group and Platelet rich plasma group.

Discussion

The present study was planned to evaluate the efficacy of LR-PRP injections as compared to standard regimen injections with corticosteroid in the treatment of plantar fasciitis. Steroid injections are not the treatment of choice as it has been reported to cause loss of cushioning due to fat pad atrophy and also can lead to osteomyelitis of the calcaneus [5]. PRP injections are being effectively used in treatment of plantar fasciitis. LR-PRP has been found to be rich in various growth factors which mediate tissue repair and anti-inflammatory property. To name a few factors found include Platelet-Derived Growth Factor (PDGF), Epidermal Growth Factor (EGF), transforming growth factor-beta 1, Vascular Endothelial Growth Factor (VEGF), basic Fibroblast Growth Factor (FGF), Hepatocyte Growth Factor (HGF), and Insulin-Like Growth Factor (ILGF) [18,24]. These growth factors are involved in modulating neo-vascularization and angiogenesis, promote mitogenesis, boost local collagen production, and provide anti-inflammatory effects by blocking cylco-oxygenase-2 enzyme production [24, 25]. Various studies have shown the efficacy of PRP therapy in plantar fasciitis. Twenty five patients with chronic plantar fasciitis treated with PRP without a control group for an average of 10.3 months reported an improvement in VAS score from 9.1 to 1.6 [26]. Another study involving 2 non-randomized group of 30 subjects on PRP and methylprednisolone reported mean VAS Scores to have improved from 6.2 to 3.2 in the steroid group and 7.33 to 3.93 in the PRP group after 6 months of treatment [27].

In the present study we observed steroid injections in plantar fasciitis to reduce pain significantly following the injections during 1 & 4 weeks as per the VAS and Nirschl stage. Whereas on the long term i.e: 12 weeks and 6 month there was no significant reduction in pain. This was in line with the study on 40 patients with plantar fasciitis treated with LR-PRP and Depo Medrol cortisone. The steroid group in this study also showed a fall in pain parameters immediately following the therapy but its long term efficacy was not significant as compared to LR- PRP group [25]. In the present study it was also observed that LR-PRP injections were slow in reducing the pain but was more effective in preventing any relapse in the long run. Despite the fact that it took more time for the LR-PRP injections to bring a significant change in pain score, it was more effective in long run as 90 % of patients reported to be completely relieved of pain, where as in the steroid group only 46.6% were relieved of pain in the 6 month study period. LR-PRP technique for plantar fasciitis offers a better treatment as its application is minimally traumatic, has a reduced risk for immune-mediated rejection, devoid of potential complications such as hypoglycemia, skin atrophy, fascia rupture that is associated with steroid injections. The study offers encouraging results of an alternative treatment that addresses the pathophysiology of plantar fasciitis that has failed traditional non-surgical modalities

Conclusion

From the present study it can be concluded that LR-PRP injections is an effective modality for managing pain in patients with plantar fasciitis in the long run, with no adverse effects as it involves autologous transfusion of platelet rich plasma. The limitation of this study is that the functional outcome was not evaluated**.** However, Studies with a longer study duration is needed, and also studies which highlight the frequency of injection is also the need of the hour.

Conflict of Interest

None declared

Acknowledgements

None

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